- WELCH (WM H.) With the authoris compliments.
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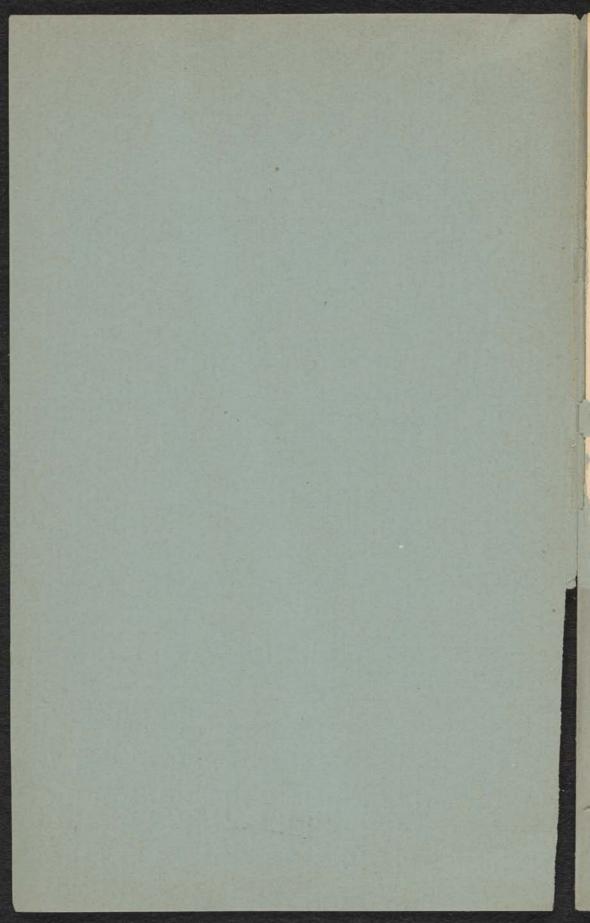
PRELIMINARY REPORT OF INVESTIGATIONS CONCERNING THE CAUSATION OF HOG CHOLERA.

By Professor William H. Welch, M. D.

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PRELIMINARY REPORT OF INVESTIGATIONS CONCERNING THE CAUSATION OF HOG CHOLERA.

By Professor William H. Welch, M. D.

Investigations of the epizootic diseases of swine, occurring in the neighborhood of Baltimore, have been made by the writer, with the coöperation of A. W. Clement, V. S., and F. L. Russell, V. S.,* in the Pathological Laboratory of the Johns Hopkins University during the past two years. We have examined about fifty hogs, from six herds, affected with hog cholera, as well as several isolated cases. In this communication, which must necessarily be brief, only a summary of the most important results will be given, a fuller report being in preparation for the volume of studies from the Pathological Laboratory, to be issued by the Johns Hopkins Hospital.

The most common and characteristic lesions consisted in superficial and deep necroses, either circumscribed or diffuse, of the inflamed mucous and other coats of the large intestine, associated often with superficial branny diphtheritic exudation. Similar necroses were occasionally found in the stomach and small intestine, in the mouth, palate and epiglottis, and less frequently in the gall bladder, bile ducts and preputial sac. Some form of pneumonia was usually, although not constantly, present. In a few cases pneumonia was present without intestinal lesions, more frequently intestinal lesions were observed with little or no pneumonia. Strongyles in the bronchi were rarely missed. Bronchitis was the rule. Pleurisy was common; pericarditis and peritonitis were present in the minority of cases. Redness of the skin was common, but inconstant. The subcutaneous, mediastinal and abdominal lymph-glands were usually swollen and reddened, chiefly in the periphery. The spleen was often normal, but in many cases was moderately and sometimes extremely swollen. The kidneys were either normal or the seat of hemorrhages and of parenchymatous degeneration or nephritis. The liver was often normal, but sometimes it presented necrotic areas. Ecchymoses were often observed in the gastric and intestinal mucosa and beneath the epi- and endo- cardium. In some cases all of the organs of the body were studded with small hemorrhages.

The bacteriological examination consisted in the study of cover-glass preparations from the different parts of the body, in the inoculation of animals, either white mice or rabbits, with parts of the lung, spleen, liver, intestine and sometimes other organs, and in the preparation of Esmarch

^{*}F. L. Russell was associated with us in the work for about one year.



roll cultures, usually of agar, from the blood, intestinal contents and all of

the principal organs of the body.

Of the bacteria isolated in pure culture and observed in microscopical preparations of the tissues only two species were sufficiently common or had such distribution as to suggest an etiological relation to the disease. These are the so-called hog cholera bacillus and the swine plague bacillus, the former first described in the Report of the Bureau of Animal Industry for 1885 as the bacterium of swine plague and in the report for 1886 as the bacterium of hog cholera, a change of nomenclature due to the detection in certain diseased swine in this country of the latter organism which now received the name of the bacterium of swine plague, as it was believed to be identical with the micro-organism previously described by Löffler and by Schütz as the specific cause of Schweine-Seuche in Germany.

The bacilli of hog cholera are short rods with rounded ends, averaging $1 \mu - 2 \mu$ in length and about 0.6μ in breadth, but forms both longer and shorter than these measurements may occur. They are very actively motile. They grow readily on all of the ordinary culture media and best at temperatures between 30° and 38° C. They do not liquefy gelatine. The growth on gelatine and on agar has a greyish or whitish color, often with a bluish translucence. Bouillon cultures present a diffuse cloudiness with whitish sediment and without surface membrane. The growth on potatoe assumes generally a brownish or yellowish tint, but it may be white, and sometimes is indistinct, although microscopically the growth is abundant. The bacilli are killed by exposure for 10 minutes to a temperature of 58° C. In cover glass preparations, from the fresh juices and tissues of animals dead of hog cholera the bacilli stain readily, and for the most part uniformly, with aniline oil gentian-violet. If the stained specimen be treated with acetic acid, many of the bacilli appear with clear centre and stained margin, which may be either uniform or slightly thicker at the poles, as described in the Reports of the Bureau of Animal Industry. Some may present a typical polar staining, but we do not regard them as good polar staining bacilli, like those of swine plague. Various irregularities in staining appear in old cultures.

The hog cholera bacilli are pathogenic for rabbits, mice, guinea-pigs and pigeons. We shall describe here only the experiments with rabbits. These animals when inoculated subcutaneously with a platinum loop from a pure culture of hog cholera bacilli die usually in from 6 to 8 days, but the duration of life may be shorter or longer. There is generally considerable dry purulent infiltration at the seat of inoculation, the subcutaneous lymphatic glands on the same side are enlarged and often present necrotic foci; the spleen is swollen, as a rule extremely, and of a dark red color and firm consistence, the liver generally presents yellowish-white streaks and dots, the heart muscle is fatty and in some cases ecchymoses, necrotic patches and diphtheritic exudation may be found in the intestinal mucosa. The bacilli, which often occur in clumps, are found most abundantly at the seat of inoculation, in the affected lymph-glands, the spleen and the liver, and are often so scanty in the blood as to escape detection by microscopical examination. We have confirmed the statements in the Reports of the Bureau of Animal Industry of the effects of these bacilli when inoculated in pigeons.

The swine plague bacilli are shorter than the hog cholera bacilli. Measuring on the average 0.8 to 1.4 μ in length, they may be very small and present the appearance of slightly oval bodies more like cocci than bacilli, or on the other hand they may present themselves as rods of considerable length. In appearance and other properties they belong to the same group of organisms as the well known bacteria of chicken cholera and of rabbit septicaemia. They are devoid of independent motion. They grow on the ordinary culture media, with the exception of potatoe, but at ordinary temperatures the growth is less rapid and abundant than that of the hog cholera bacilli. They do not liquefy gelatine. On gelatine and agar the growth is greyish, translucent, not extending far from the point of inoculation. Bouillon cultures are sometimes diffusely cloudy but more frequently the growth is in the form of a whitish, rather viscid sediment, or in little specks, with clear fluid. When planted on potatoe there may be a feeble invisible growth for one or two generations, probably due to the transference of a little nutritive medium to the potatoe with the organisms. We have not been able to cultivate them for several generations upon potatoe. They are killed at a temperature slightly lower than that destructive to hog cholera bacilli and their vitality in cultures is much shorter than that of hog cholera bacilli. In cover-glass preparations from the fresh juices and tissues of animals dead of swine-plague inoculations the bacilli present an exquisite and typical polar staining, unless the forms are very short, when the staining is uniform. They are pathogenic for rabbits, mice, guinea-pigs, pigeons and bats. We have met two degrees of virulence in this organism. The one kind kills rabbits in from 16 to 30 hours with enormous multiplication of the bacilli in the blood and organs; the other kind destroys life in from 2 to 6 days, occasionally longer, with extensive purulent and serous infiltration at the seat of inoculation, often with peritonitis, and with frequently few bacteria in the blood and organs but an immense number in the inflammatory exudates.

Regarding the distribution in the diseased hog of these two species of bacteria, great variety exists, which cannot be fully described in this short communication. In some cases the hog cholera bacilli have been found abundantly in the blood, intestine and all of the organs, in other cases they have been present only in certain parts, most frequently the spleen and liver, and absent in other parts. They may be absent from the spleen when abundant elsewhere, as in the kidney.

The swine plague bacilli, when present, likewise vary in different cases in their distribution. They are most frequently found in hepatized areas in the lungs, but they may also exist in the intestine, the blood and various organs.

As regards the frequency with which each of these organisms has been found in the diseased hogs we have met the following groups of cases: first, herds of diseased swine in which only the hog cholera bacillus has been found; second, herds in which only the swine plague bacillus was present; third, herds in which both the hog cholera bacillus and the swine plague bacillus were present in the same animal, or the hog cholera bacillus in some animals and the swine plague bacillus in others of the same herd. We have met a few, chiefly scattered, cases in which neither the hog cholera nor the swine plague bacillus was found.

We have not been able to establish any constant anatomical differences between the cases in which the swine plague bacilli alone were present and those in which only hog cholera bacilli or both organisms were found. While we have frequently found only the swine plague bacilli in extensive hepatized areas in the lungs, we have also sometimes found the hog cholera bacilli alone in apparently similar pneumonias. We have not met any epizootic corresponding to the German Schweine-Seuche in which pneumonia existed in any large number of cases without intestinal lesions.

With these results we naturally looked with especial interest to the effects of inoculation of healthy hogs with pure cultures of each of these organisms. The most stringent precautions were taken in the selection

and care of the experimental hogs.

Two hogs, weighing about 75 lbs., not subjected to any preliminary treatment, were fed each 225 cc. of bouillon culture of hog cholera bacilli. The one died in 4 and the other in $8\frac{1}{2}$ days with extensive diphtheritic inflammation and superficial circumscribed necroses of the large intestine, with moderate swelling of the spleen and of the lymphatic glands, and with ecchymoses in the lungs and elsewhere. Strongyles were present in the bronchi but there was no pneumonia. Hog cholera bacilli were found in abundance in the blood, intestine and organs. In a third hog 6.5 cc. of the same bouillon culture were injected with antiseptic precautions into the duodenum. Death occurred in 7 days with the same lesions as in the preceding hogs. Two hogs exposed in the same pen with the first hog were sick for a number of days and gradually recovered. These, when killed, presented undoubted evidence of the previous existence of acute diphtheritic inflammation of the large intestine.

The injection into the thigh and into the lung of 5 cc. of the same bouillon culture in two other hogs produced only localized sloughs with slight constitutional disturbance. The hogs were killed at the end of five weeks and hog cholera bacilli were found alive in the sloughs but none elsewhere in the

body.

The injection into the right lung of a pig of 8 cc. of a pure bouillon culture of swine plague bacilli was followed in 48-60 hours by death with extensive pneumonia, double fibrinous pleurisy, pericarditis and peritonitis and with very abundant swine plague bacilli in the exudates, the blood and the organs. Intestinal lesions were absent. The injection of 0.5 cc. bouillon culture of swine plague bacilli into each lung of another pig was followed by great rapidity and difficulty of respiration and coughing. The animal was killed at the end of a week. Double sero-fibrinous pleurisy and pericarditis and foci of pneumonia were found. The swine plague bacilli were present in abundance. The injection of pure cultures of swine plague bacilli with a fine hypodermic needle into the peritoneal cavity was not followed by any manifest effects, but in two cases in which laparotomy was performed with antiseptic precautions and pure cultures of swine plague bacilli (6.5 cc.) were injected into the duodenum the animals died in from 16 to 30 hours with acute diffuse peritonitis, pleurisy and pericarditis and enormous number of swine plague bacteria in the exudates, blood and organs; but without intestinal lesions. Doubtless some of the culture escaped into the peritoneal cavity. Subcutaneous inoculations in two cases and feeding in four cases of swine plague cultures produced no lesions, save localized abscesses and sloughs after the injections.

It is evident from these experiments, which, together with others, will be reported more fully hereafter, that both the hog cholera bacilli and the swine plague bacilli are pathogenic for swine, that the former when fed or injected into the duodenum, even in comparatively small quantity, are capable of producing intense diphtheritic inflammation and necrosis of the large intestine with general infection and the latter when injected into the thoracic cavity or into the injured peritoneal cavity of causing pneumonia and inflammation of serous membranes.

If, as seems probable, from these observations and experiments the hog cholera bacilli are to be regarded as the cause of hog cholera, at least of the intestinal lesions, how are we to explain the failure to find these bacilli in a number of cases of the disease. A number of possibilities suggest themselves. First, the bacilli may be confined to the intestine and mixed with so many other bacteria that it is difficult or impossible to isolate them. Their morphology and the appearance of their colonies are so little characteristic that this might readily happen. That this, however, cannot always be the explanation, is evident from the fact that, in several instances, rabbits inoculated with typical necrotic buttons have survived, and cultures and inoculations from other organs have failed to reveal the bacilli of hog cholera. Second, the bacilli may be confined to the intestine, and so modified that they fail to kill rabbits when inoculated subcutaneously. These bacilli appear to vary somewhat in their virulence and the possibility suggested can not at present be disproven. Third, as in cases of typhoid fever and croupous pneumonia in human beings, the specific bacilli may disappear in the later stages of the disease. This explanation, which is suggested in the Reports of the Bureau of Animal Industry, seems to us probable, but as already mentioned we have not been able to distinguish anatomically cases in which hog cholera bacilli could not be detected from some of those in which they were present.

It is not clear to us what role is to be assigned to the swine plague bacilli in the natural infections which we have studied. The facts that experimentally the swine plague bacillus is capable of causing extensive pneumonia and inflammations of serous membanes and that epizootics occur in swine in Germany with these as the predominant lesions without intestinal disease, suggest that this organism, which is apparently identical with that of the German Schweine-Seuche, is also the cause of a similar affection in this country. We are not, however, aware that any swine epizootic of pneumonia without any intestinal lesions and with the sole presence of the swine plague bacillus has been observed in this country, although cases of this description occur scattered in epizootics of hog cholera with intestinal lesions. Until such an epizootic is observed in this country it is not likely that the question will be thoroughly elucidated as to the role of the swine plague bacilli. It is possible that the swine plague bacilli are frequently present in the mouth, the air passages or the intestine of healthy hogs, analogous to the frequent presence of the micrococcus of sputum-septicaemia and of pneumonia in the mouth of human beings, and that in the mixed infections which we have observed the wide spread diffusion of the swine plague bacilli is due to secondary invasion following infection with the hog cholera bacilli. This, however, does not remove the grave significance of the swine plague bacilli, which certainly can not be ignored in our studies in this country of the diseases known as hog cholera or swine plague.

While differing in some points from the conclusions reached by the workers on this subject in the Bureau of Animal Industry, we take pleasure in recording the essential harmony of our observations with the facts which they have observed in their painstaking and creditable investigations of this difficult subject as reported since the year 1885.

Through the kindness of Dr. F. S. Billings we have had the opportunity of examining a number of cultures from diseased swine in Nebraska, chiefly direct cultures from the spleen. These in nearly all instances were pure cultures of the hog cholera bacillus. Much confusion has resulted from Dr. Billings' attempt to identify this organism with that of Schweine-Seuche.

We have had the opportunity of examining cultures of Schweine-Seuche and also of the Scandinavian swine pest, obtained from the Hygienic Institute in Berlin. The organism in the Schweine-Seuche cultures is apparently identical with the swine plague bacillus which we have isolated. The organism in the swine pest cultures is a different species of bacillus, and appears to resemble closely, if it is not identical with, the hog choléra bacillus.

We regard it of importance that the future study of swine affected with hog cholera or swine plague should be accompanied with a more thorough bacteriological examination of each case than has hitherto been customary. The mere production of a direct stab culture from one organ, such as the spleen, or the mere inoculation of an animal with material from one organ affords very incomplete and unsatisfactory information. So long as the relations of the two organisms, the hog cholera bacillus and the swine plague bacillus, to the diseases of swine are not thoroughly clear, it seems to us necessary to make Esmarch or plate cultures from the blood, the intestine and the principal organs of the body, and also to inoculate animals with material from the lungs, spleen, intestine, etc. The full report of our cases will make clear the value of both of these procedures. A single case thoroughly investigated according to modern bacteriological methods is of more value than many cases in which only stab cultures have been made from one or two organs, or in which reliance is placed solely on the results of inoculating animals. We are also convinced that little reliance can be placed upon the results of experimental inoculations of swine with the suspected organisms of hog cholera and of swine plague in regions where the disease prevails, unless very strict precautions are taken in the selection and care of the experimental animals.

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